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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : 10/579,744
Applicant : ONICHTCHOUK
Filed : May 18, 2006
TC/A.U. : 1646
Examiner :

Docket No. : 2923-753
Customer No.: 6449
Confirmation No.: 9418

SUBMISSION OF INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Submitted herewith is a copy of the translation of the International Preliminary Report on Patentability.

In the event that any fees are due with this paper, please charge our Deposit Account No. 02-2135.

Respectfully submitted,

By

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RBM/cb

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

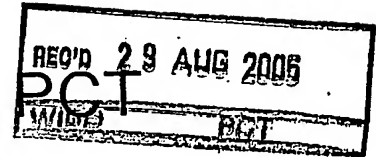
| | | |
|----------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Applicant's or agent's file reference 31993P WO | FOR FURTHER ACTION | See item 4 below |
| International application No. PCT/EP2004/013175 | International filing date (<i>day/month/year</i>) 19 November 2004 (19.11.2004) | Priority date (<i>day/month/year</i>) 19 November 2003 (19.11.2003) |
| International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237 | | |
| Applicant DEVELOGEN AKTIENGESELLSCHAFT | | |

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| 1. | This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 <i>bis</i> .1(a). | | | | | | | | | | | | | | | | | | | | | | | | |
| 2. | This REPORT consists of a total of 11 sheets, including this cover sheet. In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead. | | | | | | | | | | | | | | | | | | | | | | | | |
| 3. | <p>This report contains indications relating to the following items:</p> <table style="width: 100%;"> <tr> <td style="width: 10%; text-align: center;"><input checked="" type="checkbox"/></td> <td style="width: 40%;">Box No. I</td> <td style="width: 50%;">Basis of the report</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table> | <input checked="" type="checkbox"/> | Box No. I | Basis of the report | <input checked="" type="checkbox"/> | Box No. II | Priority | <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability | <input checked="" type="checkbox"/> | Box No. IV | Lack of unity of invention | <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | <input checked="" type="checkbox"/> | Box No. VI | Certain documents cited | <input type="checkbox"/> | Box No. VII | Certain defects in the international application | <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report | | | | | | | | | | | | | | | | | | | | | | | |
| <input checked="" type="checkbox"/> | Box No. II | Priority | | | | | | | | | | | | | | | | | | | | | | | |
| <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability | | | | | | | | | | | | | | | | | | | | | | | |
| <input checked="" type="checkbox"/> | Box No. IV | Lack of unity of invention | | | | | | | | | | | | | | | | | | | | | | | |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | | | | | | | | | | | | | | | | | | | | | | | |
| <input checked="" type="checkbox"/> | Box No. VI | Certain documents cited | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application | | | | | | | | | | | | | | | | | | | | | | | |
| 4. | The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2). | | | | | | | | | | | | | | | | | | | | | | | | |

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|-----------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------|
| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland | Date of issuance of this report 22 May 2006 (22.05.2006) |
| Facsimile No. +41 22 740 14 35 | Authorized officer <div style="text-align: center; font-weight: bold;">Yolaine Cussac</div> |
| Telephone No. +41 22 338 70 80 | |

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY



To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2004/013175

International filing date (day/month/year)
19.11.2004

Priority date (day/month/year)
19.11.2003

International Patent Classification (IPC) or both national classification and IPC
A61K38/17, C12N5/10, A01K67/027, G01N33/50, C12Q1/68, A61P3/00

Applicant
DEVELOGEN AG FÜR ENTWICKLUNGSBIOLOGISCHE FORSCHUNG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
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Authorized Officer

Fayos, C

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/013175

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☒ a sequence listing
☒ table(s) related to the sequence listing
 - b. format of material:
☒ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☒ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/013175

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial
applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-41

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-41 are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

☒ the claims, or said claims Nos. 1-41 are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/013175

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
- ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☒ not paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
 see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-41 (partially)

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|---|
| Novelty (N) | Yes: Claims | - |
| | No: Claims | - |
| Inventive step (IS) | Yes: Claims | - |
| | No: Claims | - |
| Industrial applicability (IA) | Yes: Claims | - |
| | No: Claims | - |

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/013175

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)
and /or
2. Non-written disclosures (Rules 43*bis*.1 and 70.9)
see form 210

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2004/013175

Re Item II

Priority

- 1- The current assessment is based on the assumption that all claims enjoy priority rights from the filing date of the priority document. If it later turns out that is not correct, the documents D1, D2 cited in the international search report could become relevant.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

- 2- Claims 1-41 lack clarity, support and disclosure, contrary to Arts. 6 and 5 PCT, since the subject matter for which protection is sought is not appropriately defined and the skilled person, after reading the description, would not be able to perform the invention over the whole area claimed without undue burden and without needing inventive skill. The present application does not provide any precise definition of any of SF1-SF8 (references to Genbank accession numbers, which might be modified, are not allowable). None of the references of the present application provide sufficient information to the skilled man to precisely identify the proteins which are claimed.

These claims are so called "reach-through" claims wherein protection is sought for embodiments not yet identified (no structural definition (in the form of DNA or amino acid sequence) has been provided for the claimed compounds).

Hence, no opinion with regards to novelty, inventive step and industrial applicability is to be formulated with regards to the subject matter of present claims 1-41 which do not meet the requirements of Arts. 6 and 5 PCT.

Re Item IV

Lack of unity of invention

- 3- The International Preliminary Examination Authority considers that the present application relates to the following separate inventions or groups of inventions which are

not so linked as to form a single inventive concept (Rule 13.1 PCT):

I: claims 1-41 (partially)

A pharmaceutical composition comprising SF1, its use for the treatment of pancreatic diseases, obesity, metabolic syndrome and / or other metabolic diseases or dysfunctions, its use in identification / screening methods, a non human transgenic animal or recombinant host cell exhibiting a modified expression of SF1.

II: claims 1-41 (partially)

A pharmaceutical composition comprising SF2, its use for the treatment of pancreatic diseases, obesity, metabolic syndrome and / or other metabolic diseases or dysfunctions, its use in identification / screening methods, a non human transgenic animal or recombinant host cell exhibiting a modified expression of SF2.

III: claims 1-41 (partially)

A pharmaceutical composition comprising SF3, its use for the treatment of pancreatic diseases, obesity, metabolic syndrome and / or other metabolic diseases or dysfunctions, its use in identification / screening methods, a non human transgenic animal or recombinant host cell exhibiting a modified expression of SF3.

IV: claims 1-41 (partially)

A pharmaceutical composition comprising SF4, its use for the treatment of pancreatic diseases, obesity, metabolic syndrome and / or other metabolic diseases or dysfunctions, its use in identification / screening methods, a non human transgenic animal or recombinant host cell exhibiting a modified expression of SF4.

V: claims 1-41 (partially)

A pharmaceutical composition comprising SF5, its use for the treatment of pancreatic diseases, obesity, metabolic syndrome and / or other metabolic diseases or dysfunctions, its use in identification / screening methods, a non human transgenic animal or recombinant host cell exhibiting a modified expression of SF5.

VI: claims 1-41 (partially)

A pharmaceutical composition comprising SF6, its use for the treatment of pancreatic diseases, obesity, metabolic syndrome and / or other metabolic diseases or dysfunctions, its use in identification / screening methods, a non human transgenic animal or recombinant host cell exhibiting a modified expression of SF6.

VII: claims 1-41 (partially)

A pharmaceutical composition comprising SF7, its use for the treatment of pancreatic

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2004/013175

diseases, obesity, metabolic syndrome and / or other metabolic diseases or dysfunctions, its use in identification / screening methods, a non human transgenic animal or recombinant host cell exhibiting a modified expression of SF7.

VIII: claims 1-41 (partially)

A pharmaceutical composition comprising SF8, its use for the treatment of pancreatic diseases, obesity, metabolic syndrome and / or other metabolic diseases or dysfunctions, its use in identification / screening methods, a non human transgenic animal or recombinant host cell exhibiting a modified expression of SF8.

IX: claims 1-24 (partially)

A pharmaceutical composition comprising an effector / modulator of any of SF1-SF8, its use for the treatment of pancreatic diseases, obesity, metabolic syndrome and / or other metabolic diseases or dysfunctions.

3.1- They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

The present application is concerned with pharmaceutical compositions comprising any of SF1-SF8 and / or an effector modulator thereof, its use for the treatment of pancreatic diseases, obesity, metabolic syndrome and / or other metabolic diseases or dysfunctions, as well as the use of any of SF1-SF8 in identification / screening methods, and non human transgenic animal or recombinant host cell exhibiting a modified expression of any of SF1-SF8.

SF1, SF2, SF3, SF4, SF5, SF6, SF7, SF8 do not share any common chemical structure whatsoever (other than the fact that all of them are proteins, which is already known), so that each of SF1-SF8 needs to be searched separately. Furthermore, the term "an effector / modulator" of any of SF1-SF8 encompasses a high number of compounds which neither share a common chemical structure among them, nor with any of SF1-SF8.

In addition, the following is to be noted:

The problem posed in the present application can be seen as providing pharmaceutical compositions comprising secreted factors expressed in the pancreas.

The solution according to the applicant can be any of SF1-SF8 and / or an effector /

modulator thereof.

Pharmaceutical compositions comprising SF-3 (F-spondin) are known (see e.g. D5 or D7). Furthermore, a transgenic animal expressing SF-5 (=MFG-E8) is also well known (see e.g. D6). Recombinant cells expressing SF-5 are also known from D4. Finally, the compounds of table 1 are also well known as therapeutic agents too.

Therefore, the ISA is unable to identify any common inventive concept between the various subject matters 1-9 listed above.

Searching the additional groups of agents SF2-SF8 would have required major additional searching effort. No meaningful search can be carried out for an effector / modulator of any of SF1-SF8.

Hence, the present application comprises the 9 different subject matters listed above.

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

4- Reference is made to the following documents:

- D1: WO 2004/087194 A (DEVELOGEN AKTIENGESELLSCHAFT FUER ENTWICKLUNGSBIOLOGISCHE FORSCHUNG; O) 14 October 2004 (2004-10-14)
- D2: CRAS-MÉNEUR C ET AL: "An expression profile of human pancreatic islet mRNAs by Serial Analysis of Gene Expression (SAGE)." DIABETOLOGIA. FEB 2004, vol. 47, no. 2, February 2004 (2004-02), pages 284-299, XP002330420 ISSN: 0012-186X
- D3: DATABASE GENBANK [Online] 10 April 2005 (2005-04-10), XP002330263 retrieved from GENBANK Database accession no. NM_026522
- D4: OSHIMA KENJI ET AL: "Secretion of a peripheral membrane protein, MFG-E8, as a complex with membrane vesicles. A POSSIBLE ROLE IN MEMBRANE SECRETION" EUROPEAN JOURNAL OF BIOCHEMISTRY, BERLIN, DE, vol. 269, no. 4, February 2002 (2002-02), pages 1209-1218, XP002233407 ISSN: 0014-2956
- D5: US-A-5 279 966 (JESSELL ET AL) 18 January 1994 (1994-01-18)

3

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2004/013175

D6: US 2002/144296 A1 (WHEELER MATTHEW B ET AL) 3 October 2002 (2002-10-03)
D7: EP-A-1 149 844 (RIKEN) 31 October 2001 (2001-10-31)
D8: KAWAMURA K ET AL: "A new family of growth factors produced by the fat body and active on *Drosophila* imaginal disc cells." DEVELOPMENT (CAMBRIDGE, ENGLAND) JAN 1999, vol. 126, no. 2, January 1999 (1999-01), pages 211-219, XP002330421 ISSN: 0950-1991

- 5- When / if carrying out amendments, and in order to facilitate the examination of the conformity of the amended application with the requirements of Article 34(2)(b) PCT, the applicant is requested to clearly identify the amendments carried out, no matter whether they concern amendments by addition, replacement or deletion, and to indicate precisely the passages of the application as filed on which these amendments are based (also rule 66.8 (a) PCT).

Only amendments with a clearly identified basis on the application as originally filed will be taken into account for the international preliminary examination report.